(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 April 2001 (26.04.2001)

PCT

(10) International Publication Number
WO 01/28623 A2

(51) International Patent Classification[7]: A61N

(21) International Application Number: PCT/US00/41226

(22) International Filing Date: 18 October 2000 (18.10.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/160,222 18 October 1999 (18.10.1999) US

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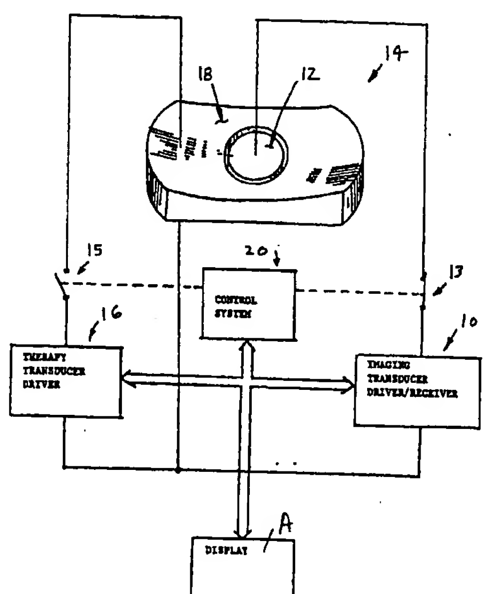
(81) Designated States (*national*): JP, US.

(84) Designated States (*regional*): European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published:
— *Without international search report and to be republished upon receipt of that report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SPLIT BEAM TRANSDUCER



(57) Abstract: A method and apparatus for treating tissue includes providing an ultrasound transducer (14) having a surrounded ultrasound generating region (12) and a surrounding ultrasound generating region (18). The surrounded region (12) and surrounding region (18) are separately actuable (10, 13, 15, 16, 20) to generate ultrasound. At least the surrounding region (18) has a focus. The ultrasound transducer (12) is placed adjacent the tissue to be treated so that the focus of the surrounding region (18) lies adjacent a treatment site. The surrounding region (18) is actuated while the surrounded region (12) is maintained unactuated to treat the tissue to create a treated region in the tissue.

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SPLIT BEAM TRANSDUCER

Field of the Invention

This invention relates to methods and apparatus for the treatment of disease. It is disclosed in the context of high-intensity focused ultrasound (hereinafter sometimes HIFU) treatment of prostate cancer. However, it is believed to be useful in other applications as well.

Background of the Invention

In HIFU treatment of benign prostatic hyperplasia (hereinafter sometimes BPH), typically only prostate tissue surrounding the urethra is ablated. This treatment results in necrosis of prostate tissue adjacent the urethra, thereby relieving symptoms of BPH. A number of systems are known for the generation of treatment-intensity ultrasound in general, and the HIFU treatment of BPH in particular. There are, for example, the systems described in U.S. Patents Nos.: 4,084,582; 4,207,901; 4,223,560; 4,227,417; 4,248,090; 4,257,271; 4,317,370; 4,325,381; 4,586,512; 4,620,546; 4,658,828; 4,664,121; 4,858,613; 4,951,653; 4,955,365; 5,036,855; 5,054,470; 5,080,102; 5,117,832; 5,149,319; 5,215,680; 5,219,401; 5,247,935; 5,295,484; 5,316,000; 5,391,197; 5,409,006; 5,443,069; 5,470,350; 5,492,126; 5,573,497; 5,601,526; 5,620,479; 5,630,837; 5,643,179; 5,676,692; and 5,840,031. It has also been suggested in the literature to use multi-element array transducer systems with different electronics timing to drive the various elements of these arrays. There are, for example: S. Umemura and C. A. Cain, "The Sector-Vortex Phased Array: Acoustic Field Synthesis for Hyperthermia," IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, vol. 36, pp. 249-257, 1989; F. L. Lizzi, M. Astor, C. Deng, A. Rosado, D. J. Coleman and R. Silverman, "Asymmetric Focussed Arrays for Ultrasonic Tumor Therapy," Proc. IEEE Ultrason. Symp., vol. 2, pp. 1281-1284, 1996; D. Daum, M. T. Buchanan, T. Field and K. Hynynen, "Design and Evaluation of a Feedback Based Phased Array System for Ultrasound Surgery," IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, vol. 45, no. 2, pp. 431-438, 1998; and, H. Wan, P. VanBaren, E. S. Ebbini and C. A. Cain, "Ultrasound Surgery: Comparison of Strategies Using

Phased Array Systems," IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, vol. 43, no. 6, pp. 1085-1098, November, 1996. The disclosures of these references are hereby incorporated herein by reference. This listing is not intended to be a representation that a thorough search has been made of the relevant art, or that no better references than those listed are available; nor should any such representation be inferred.

Near-field heating which may result from the use of these approaches requires fairly appreciable time delays for tissue in the near field to cool between ultrasound irradiation cycles. In HIFU treatment of prostate cancer, treatment of the whole prostate to eradicate all the cancerous cells and surrounding tissue are the objective. Using a single HIFU beam, such procedures to treat prostate cancer can dictate very long treatment times. There is a need to improve the treatment time for the HIFU treatment of prostate cancer, while maintaining efficacy and safety.

Disclosure of the Invention

According to one aspect of the invention, a method of treating tissue includes providing an ultrasound transducer having a surrounded ultrasound generating region and a surrounding ultrasound generating region. The surrounded region and surrounding region are separately actuable to generate ultrasound. At least the surrounding region has a focus. The ultrasound transducer is placed adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent a first treatment site. The surrounding region is actuated while the surrounded region is maintained unactuated to treat the tissue to create a first treated region in the tissue.

Illustratively according to this aspect of the invention, the method further includes moving the ultrasound transducer to another location adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent a second treatment site. The surrounding region is again actuated and the surrounded region is again maintained unactuated to treat the tissue to create a second treated region in the tissue.

According to another aspect of the invention, an apparatus for treating tissue includes an ultrasound transducer having a surrounded ultrasound generating

region and a surrounding ultrasound generating region. At least the surrounding region has a focus. The apparatus further includes a first driver for driving the surrounded region to generate ultrasound, and a second driver for driving the surrounding region to generate ultrasound. The first driver is separately actuable from the second driver and the second driver is separately actuable from the first driver. The first driver is actuable to cause the surrounded region to generate ultrasound to aid in placing the ultrasound transducer adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent the treatment site. The second driver is actuable while the surrounded region is maintained unactuated to treat the tissue to create a first treated region in the tissue.

Illustratively according to this aspect of the invention, the ultrasound transducer is adapted to be positioned at another location adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent a second treatment site, the second driver then being further actuable to cause the surrounding region to produce ultrasound while the first driver is maintained unactuated to treat the tissue to create a second treated region in the tissue.

Further illustratively according to the invention, the second treated region is at least adjacent the first treated region.

Additionally illustratively according to the invention, the second treated region intersects the first treated region.

Illustratively according to the invention, the second treated region overlaps the first treated region.

Further illustratively according to the invention, the first driver is actuable to cause the surrounded region to generate ultrasound to aid in placing the ultrasound transducer adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent the first treatment site.

Additionally illustratively according to the invention, the first driver is actuable to cause the surrounded region to generate ultrasound to aid in placing the ultrasound transducer adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent the second treatment site.

Brief Description of the Drawings

The invention may best be understood by referring to the following description and accompanying drawings which illustrate the invention. In the drawings:

Fig. 1 illustrates a partly block and partly schematic diagram of a system constructed according to the invention;

Fig. 2 illustrates a transverse beam profile image of a sharply focused single beam pattern generated using a Schlieren imaging system;

Fig. 3 illustrates a negative of a longitudinal beam profile image of a sharply focused single beam pattern generated using a Schlieren imaging system;

Fig. 4 illustrates a transverse beam profile image of a beam having a reduced amplitude main lobe with four side lobes, sometimes referred to herein as a "split beam," generated using a Schlieren imaging system;

Fig. 5 illustrates a negative of a longitudinal beam profile image of a split beam generated using a Schlieren imaging system;

Fig. 6 illustrates illustrates a simulation result for the split beam format in the focal field;

Fig. 7 illustrates illustrates a simulation result for a single beam format in the focal field;

Fig. 8 illustrates lesions created by the single beam format and the split beam format on the surface of a polyester film, side by side for purposes of comparison;

Fig. 9 illustrates temperature profiles measured by the thermocouples; and,

Fig. 10 illustrates a lesion created on the prostate gland of a test animal using a system according to the invention.

Detailed Descriptions of Illustrative Embodiments

A transducer arrangement from an existing Sonablate-200™ BHP HIFU treatment system available from Focus Surgery, Inc., 3940 Pendleton Way, Indianapolis, IN 46226, was modified as illustrated in Fig. 1 for the treatment of localized prostate cancer. The control of the imaging driver/receiver 10 which drives

the imaging transducer portion 12 of the multiple section ultrasound transducer 14 was separated, 20, 13, 15, from the control of the therapy driver 16 so that thc imaging portion 12 was not driven when the therapy portion 18 of the transducer 14 was. These changes were made in the control 20 and drive circuits 16, 10 of the treatment transducer 18 and the imaging transducer 12, respectively, to reduce the amplitude of the main beam and surround it with a number, four in the illustrated embodiment, of significant side lobes. In the split beam configuration, the HIFU beam is spread to create a larger treatment volume per ultrasound exposure which can reduce the overall treatment time.

A study was conducted to compare the necrosis volume and temperature patterns produced from single beam and split beam operating configurations. Experiments were performed on different test objects including Mylar® brand polyester film strips, Plexiglas® brand acrylic plastic sheets, *in-vitro* turkey breast tissue and *in vivo* dog prostates. (Mylar is a registered trademark of E. I. Du Pont de Nemours and Company. Plexiglas is a registered trademark of Rohm and Haas Company and ELF Atochem S. A.) The results established that the split beam configuration created larger lesion volumes for the same exposure time, while keeping the temperature near other anatomic structures and features, for example, the rectal wall, at safe levels.

This approach offers improvement over the present single beam treatment. For example, it results in a treatment which is not as time-consuming. These results are achieved by splitting the main ultrasound beam into a central, higher amplitude lobe 22 and a plurality, four in this example, of side lobes 24 of somewhat lower amplitudes. This produces total treated area in the focal plane about three times larger in this example than the prior art single higher amplitude beam 26 does. In addition, tissue heat conduction has been demonstrated to bridge the lesions created by the central lobe 22 and the side lobes 24, resulting in a larger treated volume per ultrasonic irradiation cycle. Avoidance of a single intense beam 26 can also reduce the likelihood of vapor formation at the focal site.

Computer simulations were performed to explore the effects and differences between the single lobe 26 configuration and central lobe 22-and-side lobes 24 configuration. The acoustic properties, beam patterns and power output were

verified by standard procedures. Then, *in vitro* tests in turkey breast tissue and *in vivo* experiments in dog prostate were carried out and lesion volumes created by the split beam transducer were examined. The results demonstrated that the split beam 22, 24 format creates larger volumes of lesion than the single beam 26 in turkey breast tissue and in dog prostate. For the single beam 26 format phases of the study, a step size of 1.8 mm was selected between adjacent HIFU lesions. This was done in an effort to promote connected necrosis. In the split beam 22, 24 format phases of the study, connected lesions in turkey breast tissue and in dog prostate were achieved using a step size of 2.8 mm. This resulted in a more than 30% reduction in treatment time for the same volume of tissue treatment. The results demonstrate that treatment using the split beam 22, 24 format results in larger lesion volumes than are achieved using the single beam 26 format in turkey breast tissue and also in dog prostate tissue.

Details of the construction and operation of the Sonablate-200™ system are described in, for example, N. T. Sanghvi, F. J. Fry, R. Bihrle, R. S. Foster, M. H. Phillips, J. Syrus and C. Hennige, "Non-Invasive Surgery of Prostate Tissue By High Intensity Focused Ultrasound," IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, vol. 43, no. 6, pp. 1099-1110, November, 1996, the disclosure of which is incorporated herein by reference. Briefly, the spherically focused transducer 14 of the Sonablate-200™ HIFU device contains dual elements 12, 18 on the same piezoelectric ceramic crystal. In conventional operation, the center element 12 is used in both imaging and therapy, and the outer element 18 is used in therapy. Use of the inner element 12 and outer element 18 both in therapy mode produces a sharply focused beam 26 which is sometimes referred to herein as a "single beam." However, if the center element 12 is not actuated during therapy, then a beam 22, 24 characterized by a reduced amplitude main lobe 22 with four side lobes 24 is produced when the outer element 18 is driven. Figs. 2 and 3 illustrate transverse and longitudinal beam profile images, respectively, of the sharply focused single beam 26 pattern. These images are generated using a Schlieren imaging system. Figs. 4 and 5 illustrate transverse and longitudinal beam profile images, respectively, of a split beam having a reduced amplitude main lobe 22 with four side lobes 24, as a result of driving only the outer element 18. Again, these images are generated using a Schlieren imaging system.

The beams 22, 24 and 26 were also analyzed by computer simulation using numerical integration techniques. The following parameters were used during the simulations: frequency, 4 MHz; focal length, 3.5 cm; transducer aperture, 30 mm x 22 mm; and, inner element diameter, 10 mm. Figs. 6 and 7 illustrate the simulation results for the split beam 22, 24 format and the single beam 26 format, respectively, in the focal field.

Both beam formats were also tested using Mylar® strips placed in the focal plane. The lesions created on the surface are illustrated side-by-side for purposes of comparison in Fig. 8. The power levels used are the same in both trials, namely, 30 watts. The areas treated by the split beam 22, 24 are illustrated on the left. Again, the spacing between successive treatments is 2.8mm. As illustrated, the spaces between the centers of consecutive ultrasonic treatments using the split beam 22, 24 format are characterized by the presence of lesion. Also as illustrated, there are significant gaps between the lesions on the right side of Fig. 8 where the single beam format 26 is used.

In-vitro experiments were conducted using fresh turkey breast tissue. The tissue was immersed in a water bath maintained at about 37°C temperature. About .0508 mm (about 0.002 inch) diameter thermocouples (available from Physitemp, New Jersey) were introduced, using a thin needle, into the test tissue to monitor the temperature at the entrance of the ultrasound beam into the tissue and close to the focal point. At the end of the ultrasound exposures, the tissue was sliced and the lesion sizes and shapes were measured. The individual lesions produced using the split beam format were significantly larger in size.

In order to verify the efficacy and safety of the split beam format for conducting HIFU treatment in the presence of blood perfusion, an *in vivo* animal study was conducted on male dogs using a Sonablate-200™ instrument. The animals were first anesthetized. Then an ultrasound probe of the type described was inserted rectally, as is conventional in the clinical treatment of BPH by HIFU in humans. The thermocouples were placed under real-time ultrasound guidance and temperatures were recorded using a model LT-100 sixteen-channel thermometry system available from Labthermics Inc., Champaign, IL. After the treatment was completed, the

animals were sacrificed and the prostates, bladders and adjacent sections of the rectal wall were preserved in formalin solution for histology examinations.

At the same total acoustic power (TAP) of 35watts, and focal length of 4.0cm, tissue necrosis achieved using the split beam format was wider than was achieved using the single beam format. The depths of the lesions were comparable. The lesion width at the focus achieved using the split beam format is estimated at greater than 3 mm. The temperature profiles measured by the thermocouples are illustrated in Fig. 9. Fig. 10 illustrates the lesion created on male dog prostate gland. At 2.8 mm spacing between the centers of consecutive exposures, the treatment time was reduced from one hour to thirty-five minutes. Necrosis of the treated prostate tissue volume was achieved without any rectal injury. This is believed to establish the improvement in performance and safety of the split beam format in prostate cancer treatment as compared to single beam treatment.

CLAIMS:

1. A method of treating tissue including providing an ultrasound transducer having a surrounded ultrasound generating region and a surrounding ultrasound generating region, the surrounded region and surrounding region being separately actuable to generate ultrasound, at least the surrounding region having a focus, placing the ultrasound transducer adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent a first treatment site, actuating the surrounding region and maintaining the surrounded region unactuated to treat the tissue to create a first treated region in the tissue.

2. The method of claim 1 further including moving the ultrasound transducer to another location adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent a second treatment site, actuating the surrounding region and maintaining the surrounded region unactuated to treat the tissue to create a second treated region in the tissue.

3. The method of claim 2 wherein moving the ultrasound transducer to another location so that the focus of the surrounding region lies adjacent a second treatment site includes moving the ultrasound transducer to another location adjacent the tissue to be treated so that the focus of the surrounding region lies at least adjacent the first treated region in the tissue.

4. The method of claim 3 wherein actuating the surrounding region and maintaining the surrounded region unactuated to treat the tissue to create a second treated region in the tissue includes actuating the surrounding region and maintaining the surrounded region unactuated to treat the tissue to create a second treated region which intersects the first treated region.

5. The method of claim 4 wherein actuating the surrounding region and maintaining the surrounded region unactuated to treat the tissue to create a second treated region in the tissue which intersects the first treated region includes actuating the surrounding region and maintaining the surrounded region unactuated to treat the tissue to create a second treated region which overlaps the first treated region.

6. Apparatus for treating tissue including an ultrasound transducer having a surrounded ultrasound generating region and a surrounding ultrasound

generating region, at least the surrounding region having a focus, a first driver for driving the surrounded region to generate ultrasound, a second driver for driving the surrounding region to generate ultrasound, the first driver being separately actuable from the second driver and the second driver being separately actuable from the first driver, the second driver being actuable while the surrounded region is maintained unactuated to treat the tissue to create a first treated region in the tissue.

7. The apparatus of claim 6 wherein the ultrasound transducer is adapted to be positioned at another location adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent a second treatment site, the second driver then being further actuable to cause the surrounding region to produce ultrasound while the first driver is maintained unactuated to treat the tissue to create a second treated region in the tissue.

8. The apparatus of claim 7 wherein the second treated region in the tissue is at least adjacent the first treated region.

9. The apparatus of claim 8 wherein the second treated region intersects the first treated region.

10. The apparatus of claim 9 wherein the second treated region overlaps the first treated region.

11. The method of claim 6 wherein the first driver is actuable to cause the surrounded region to generate ultrasound to aid in placing the ultrasound transducer adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent a treatment site.

12. The method of claim 7 wherein the first driver is actuable to cause the surrounded region to generate ultrasound to aid in placing the ultrasound transducer adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent the second treatment site.

13. The method of claim 8 wherein the first driver is actuable to cause the surrounded region to generate ultrasound to aid in placing the ultrasound transducer adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent the second treatment site.

14. The method of claim 9 wherein the first driver is actuable to cause the surrounded region to generate ultrasound to aid in placing the ultrasound

transducer adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent the second treatment site.

15. The method of claim 10 wherein the first driver is actuable to cause the surrounded region to generate ultrasound to aid in placing the ultrasound transducer adjacent the tissue to be treated so that the focus of the surrounding region lies adjacent the second treatment site.

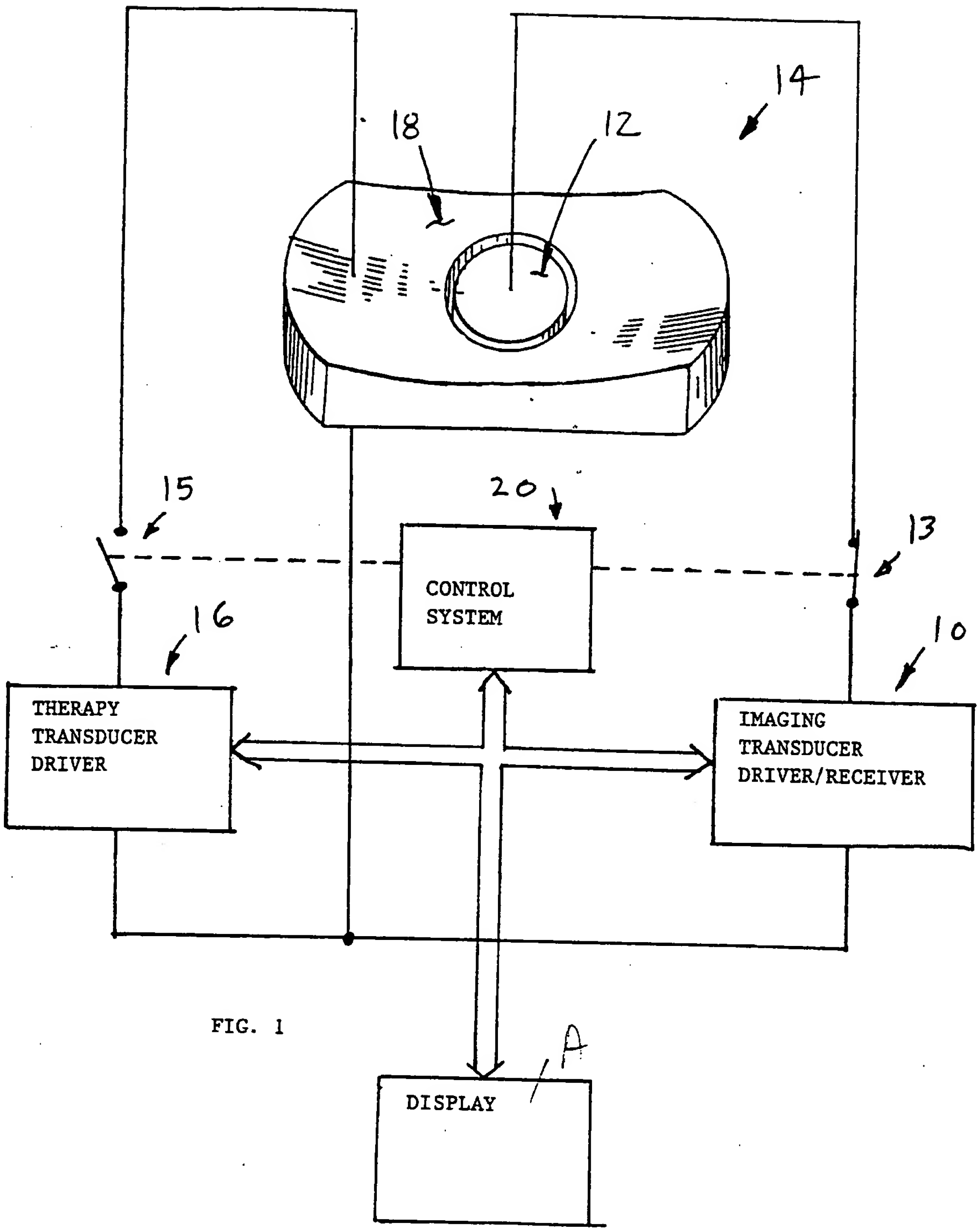
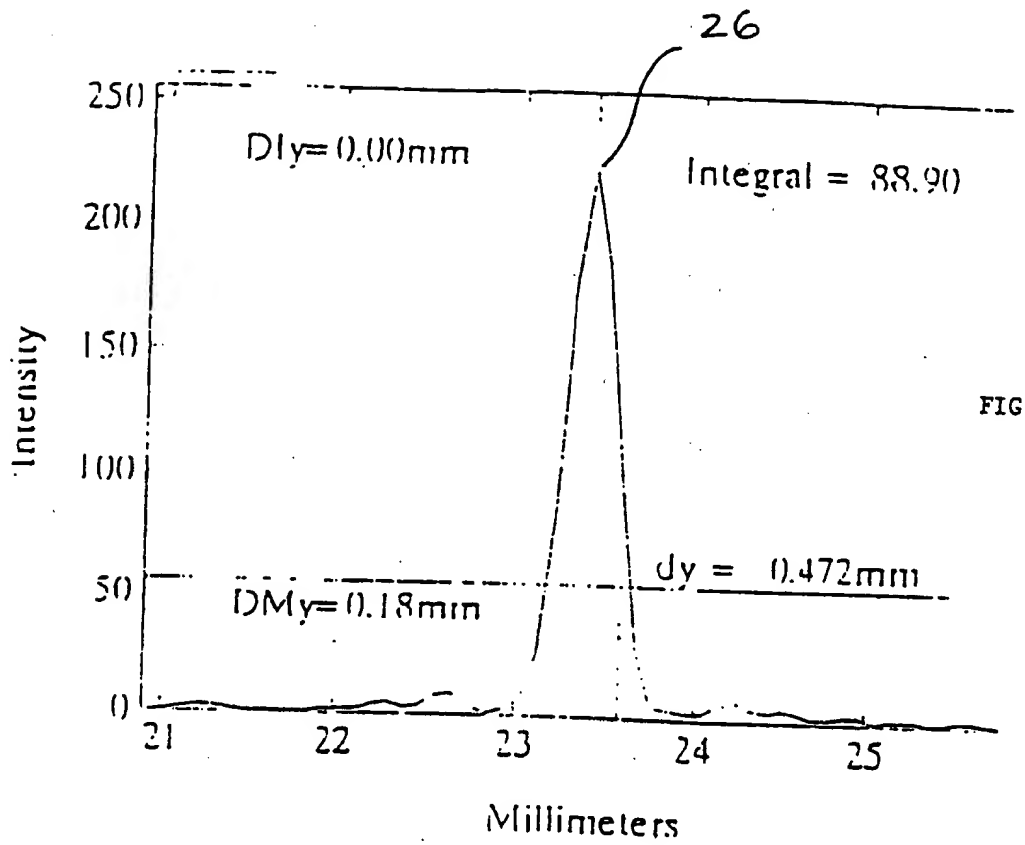

14
18
12
15
20
13
16
10
CONTROL SYSTEM
THERAPY TRANSDUCER DRIVER
IMAGING TRANSDUCER DRIVER/RECEIVER
1A
DISPLAY

FIG. 1


26
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200
150
100
50
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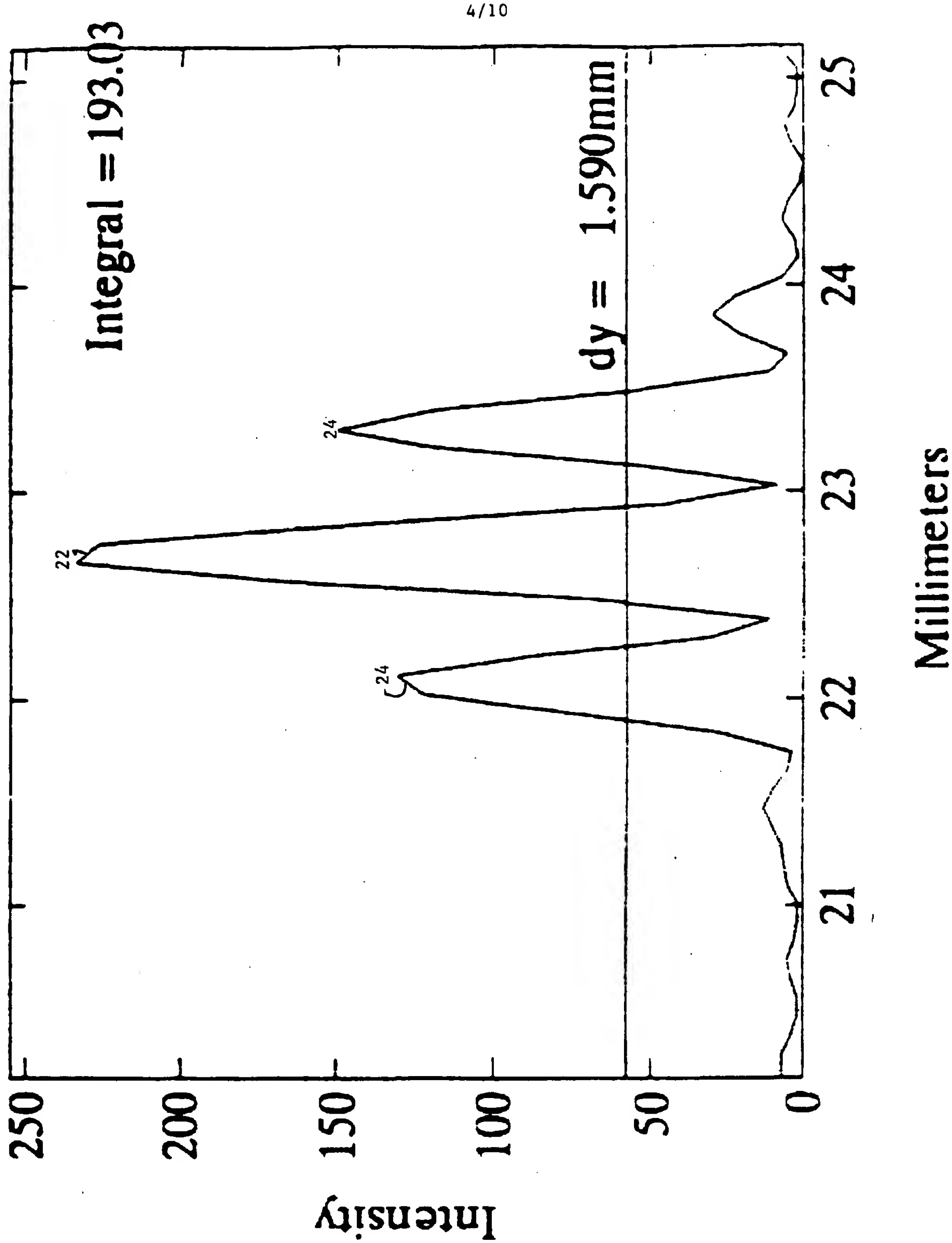
DIy=0.00mm
Integral = 88.90
dy = 0.472mm
DMy=0.18mm
21
22
23
24
25
Millimeters

FIG. 2

Fig. 3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dy = 1.590mm
Intensity
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200
150
100
50
0
Millimeters
21
22
23
24
25
22
24
24

Fig. 4

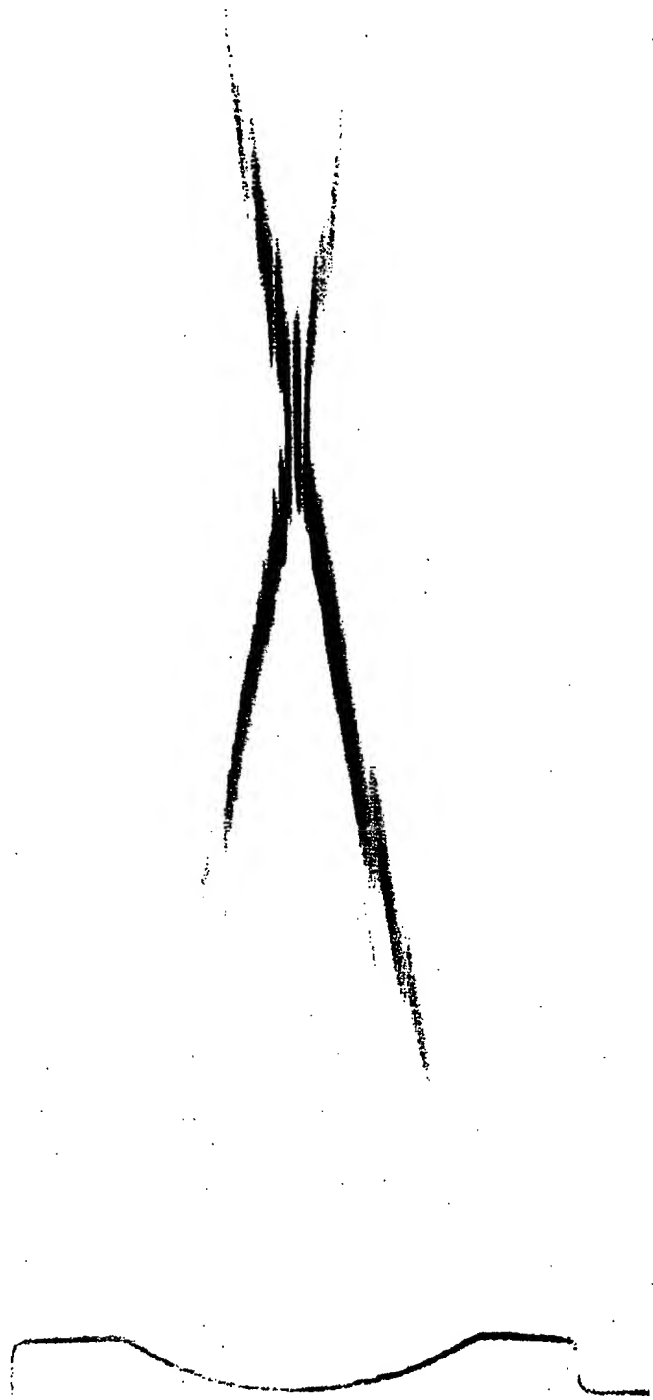
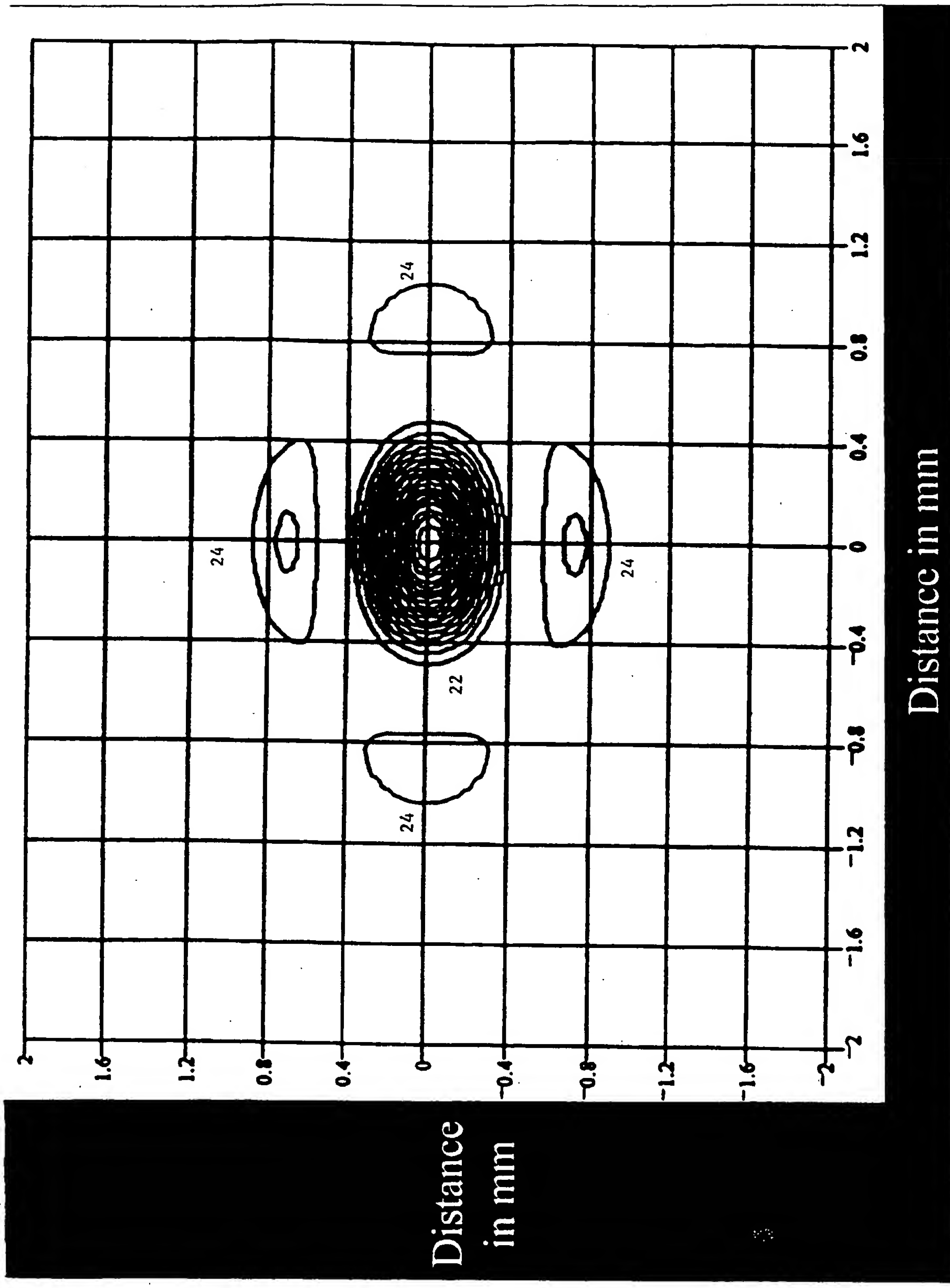


Fig. 5



Distance in mm
Distance in mm
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1.6
1.2
0.8
0.4
0
-0.4
-0.8
-1.2
-1.6
-2
24
24
24
24
22

Fig. 6

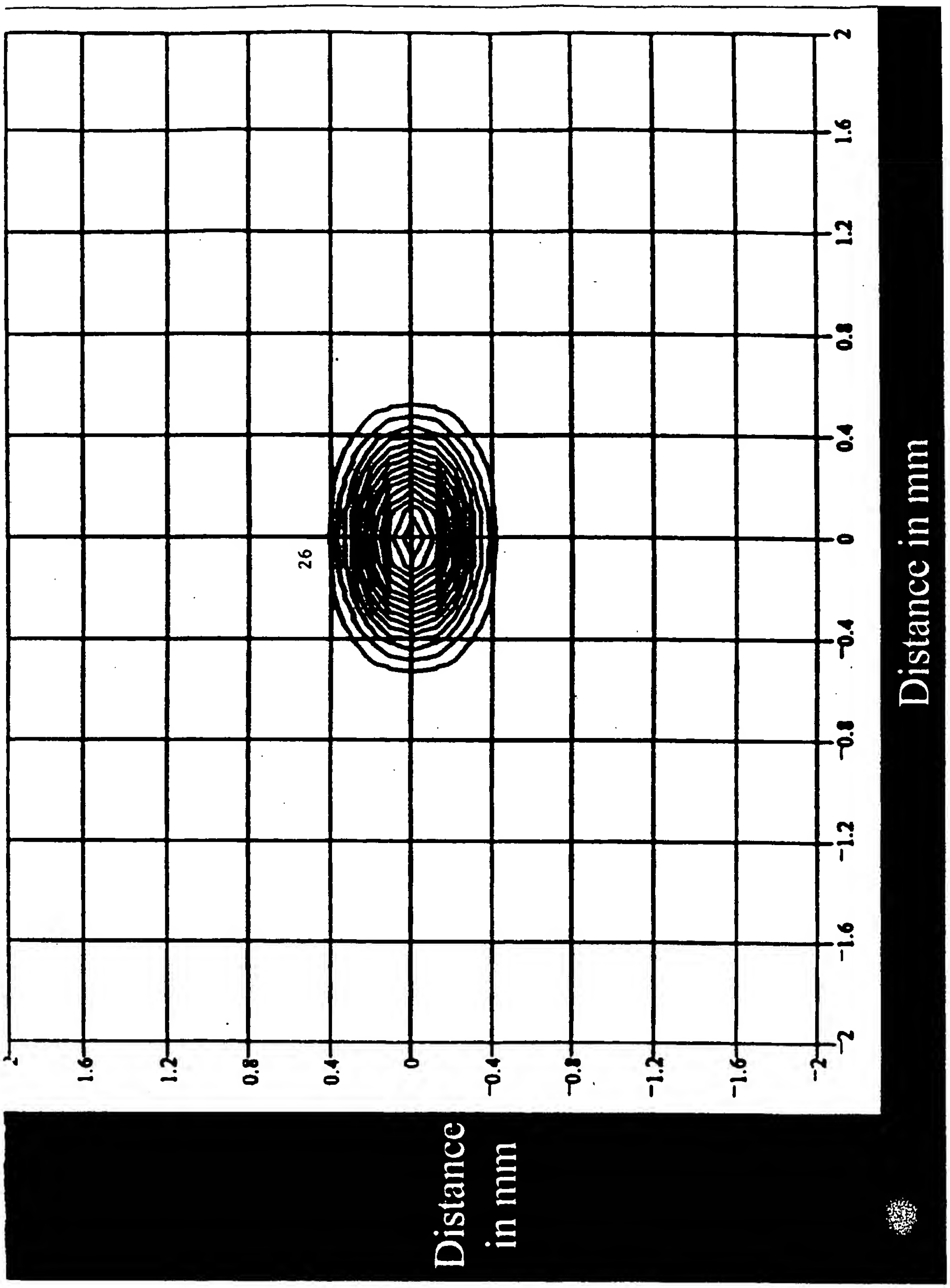

Fig. 7

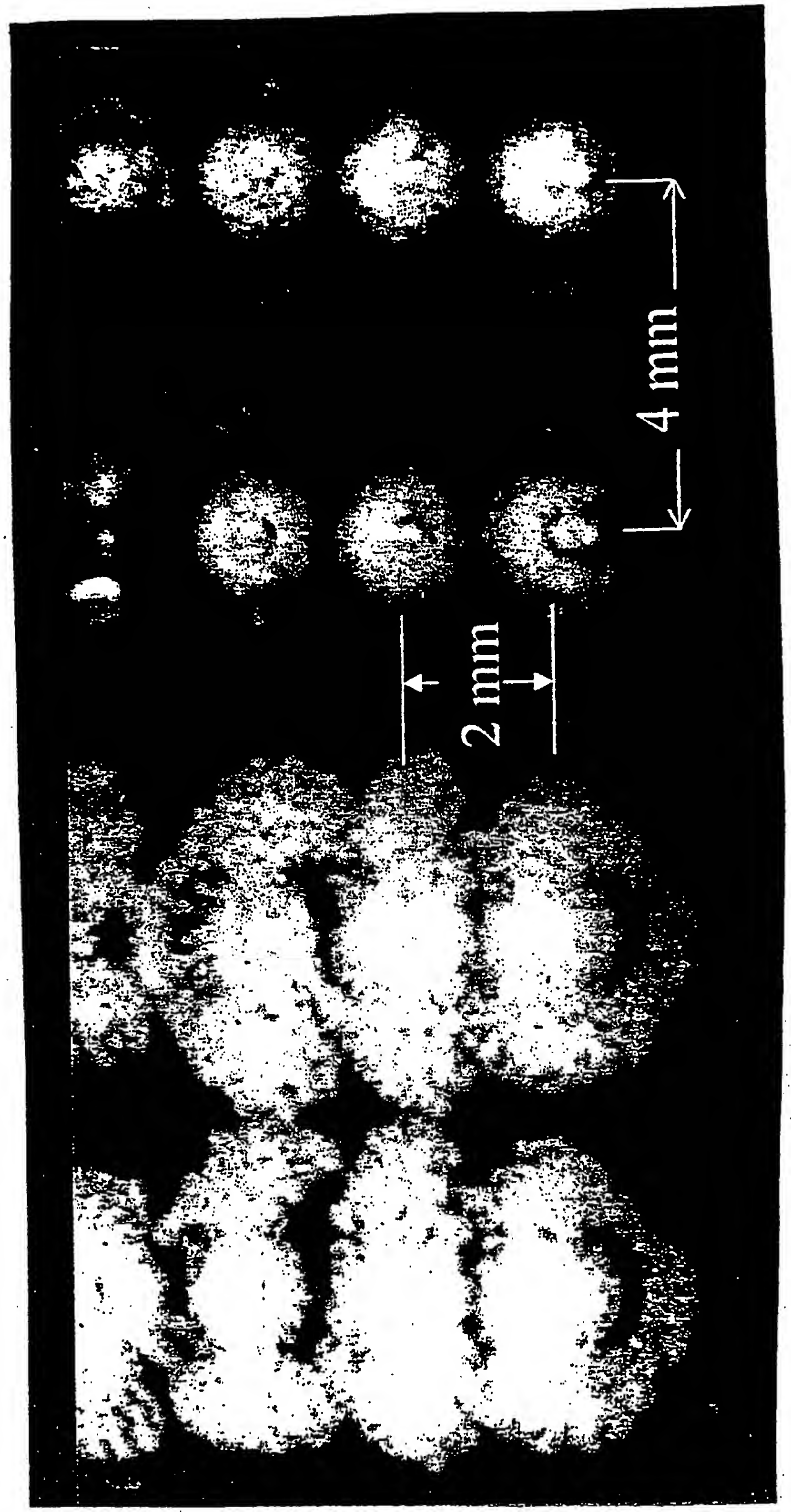

FIG. 8

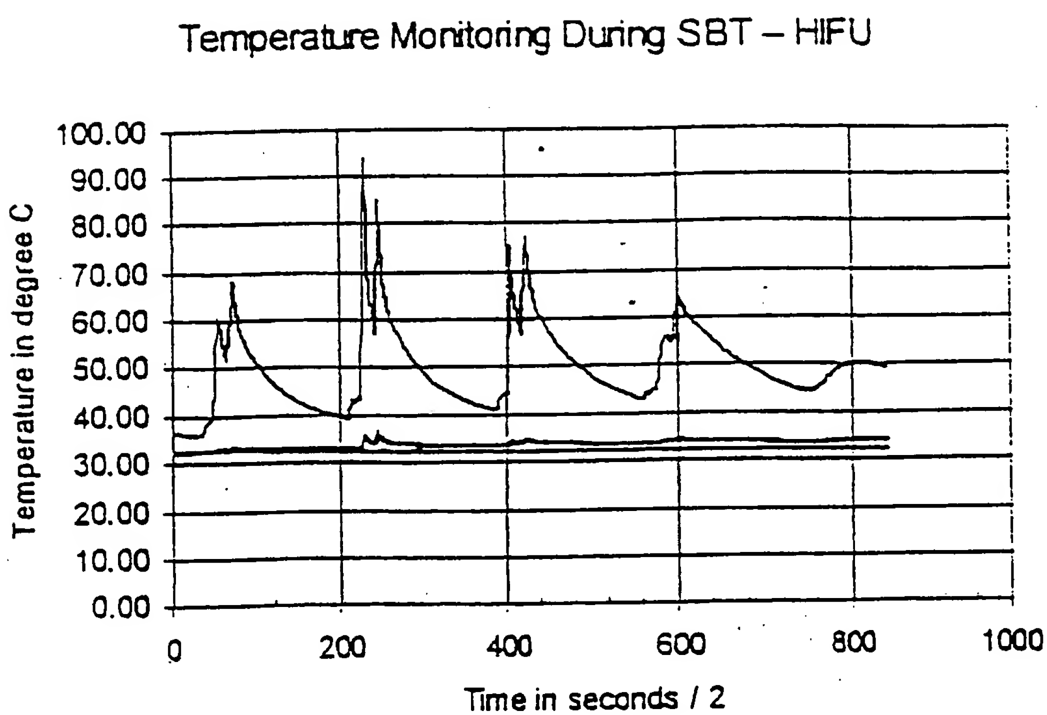
Temperature Monitoring During SBT – HIFU
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
Temperature in degree C
0
200
400
600
800
1000
Time in seconds / 2

FIG. 9

Fig. 10